

FILE 'HOME' ENTERED AT 12:48:15 ON 17 OCT 2002

=> file cancerlit, caplus, medline, embase, biosis, uspatful  
'CAPLUS' IS NOT A VALID FILE NAME  
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files  
that are available. If you have requested multiple files, you can  
specify a corrected file name or you can enter "IGNORE" to continue  
accessing the remaining file names entered.  
ENTER A FILE NAME OR (IGNORE):caplus

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		0.42	0.42

FILE 'CANCERLIT' ENTERED AT 12:49:09 ON 17 OCT 2002

FILE 'CAPLUS' ENTERED AT 12:49:09 ON 17 OCT 2002  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 12:49:09 ON 17 OCT 2002

FILE 'EMBASE' ENTERED AT 12:49:09 ON 17 OCT 2002  
COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 12:49:09 ON 17 OCT 2002  
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'USPATFULL' ENTERED AT 12:49:09 ON 17 OCT 2002  
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s tnf (w) trimers  
L1 15 TNF (W) TRIMERS

=> duplicate remove  
ENTER L# LIST OR (END):l1  
DUPLICATE PREFERENCE IS 'CANCERLIT, CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L1  
L2 6 DUPLICATE REMOVE L1 (9 DUPLICATES REMOVED)

=> d l2 1- ibib,abs  
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L2 ANSWER 1 OF 6 USPATFULL  
ACCESSION NUMBER: 1999:67160 USPATFULL  
TITLE: Nucleic acids encoding tumor virus susceptibility genes  
INVENTOR(S): Brojatsch, Jorgen, Jamaica Pond, MA, United States  
Naughton, John, Somerville, MA, United States  
Young, John A. T., Auburndale, MA, United States  
PATENT ASSIGNEE(S): President & Fellows of Harvard College, Cambridge, MA,  
United States (U.S. corporation)

NUMBER	KIND	DATE
--------	------	------

PATENT INFORMATION:	US 5912141	19990615
APPLICATION INFO.:	US 1996-651579	19960522 (8)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Feisee, Lila	
ASSISTANT EXAMINER:	Kaufman, Claire M.	
LEGAL REPRESENTATIVE:	DeConti, Jr., Giulio A.Lahive & Cockfield, LLP	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	15	
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	3582	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention concerns the discovery of a new member of the TNF receptor superfamily, referred to herein as the candidate "tvb receptor". Experimental evidence suggests that the instant gene corresponds to the gene of the tvb.sup.s3 locus responsible for mediating certain viral infection. The tvb receptor plays a functional role as the receptor for certain of the avian leukosis/sarcoma viruses (ALSV) in avians, and a likely role as a receptor for tumor viruses in other animals, e.g., the feline leukemia virus and the like. Moreover, inspection of the tvb sequence, particularly in comparison with other TNF receptors, reveals the presence of a "death domain" in the cytoplasmic tail of the tvb receptor, suggesting a role for the tvb receptor in determining tissue fate and maintenance. For instance, the tvb genes and gene products may participate, under various circumstances, in the control of proliferation, differentiation and/or cell death.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 2 OF 6 USPATFULL

ACCESSION NUMBER: 1999:15698 USPATFULL

TITLE: Compositions and methods for screening drug libraries

INVENTOR(S): Spinella, Dominic Gregory, San Diego, CA, United States  
Becherer, Kathleen Ann, San Diego, CA, United States  
Brown, Steven Joel, San Diego, CA, United States

PATENT ASSIGNEE(S): Chugai Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5866341 19990202  
APPLICATION INFO.: US 1996-627151 19960403 (8)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Achutamurthy, Ponnathapura  
LEGAL REPRESENTATIVE: Gritzmacher, Christine A., Fisher, Carlos A.  
NUMBER OF CLAIMS: 63  
EXEMPLARY CLAIM: 1  
LINE COUNT: 2082

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of screening for binding partners of a specific molecule. The method employs a chimeric protein having at least two different binding regions; one containing at least a portion of the specific molecule or an analog thereof, and the other containing a binding region of an immunoglobulin chain. In a preferred embodiment, the method is used for rapidly screening member compounds of a combinatorial library for potential biological activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 3 OF 6 CANCERLIT DUPLICATE 1

ACCESSION NUMBER: 96364112 CANCERLIT

DOCUMENT NUMBER: 96364112 PubMed ID: 8739350

TITLE: Searching for new TNF-alpha analogs having potential application in cancer therapy.

AUTHOR: Menart V; Kus B; Novakovic S; Sersa G; Gaberc-Porekar V;  
Harb V; Milicic S; Stalc A

CORPORATE SOURCE: Lek d.d., Research and Development, Ljubljana, Slovenia.

SOURCE: PFLUGERS ARCHIV. EUROPEAN JOURNAL OF PHYSIOLOGY, (1996) 431  
(6 Suppl 2) R233-4.

Journal code: 0154720. ISSN: 0031-6768.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: MEDLINE; Priority Journals

OTHER SOURCE: MEDLINE 96364112

ENTRY MONTH: 199701

ENTRY DATE: Entered STN: 19970205

Last Updated on STN: 19970509

AB Two new TNF-alpha analogs were prepared and tested for their anti-tumor

activity on fibrosarcoma SA-1 tumor model in vivo. In analog LK-801 two histidines (His107His108) were introduced into the surface loop thus enabling efficient purification by metal-affinity chromatography. This analog showed less side effects and can serve as a lead compound to look for other useful mutations. Another analog LK-802 was designed by introduction of additional pair of mutations (Cys95Cys148) into LK-801 in order to prepare disulfide linked TNF trimers.

Cytotoxicity on mouse cell line L929 was comparable to TNF-alpha, but effect on tumor growth was quite reduced. Pharmacokinetic study revealed that serum levels of LK-802 were quite low in comparison to native TNF-alpha. This at least partially explains why anti-tumor activity of LK-802 is reduced and also illustrates the problems in designing the analogs with desired in vivo biological properties.

L2 ANSWER 4 OF 6 USPATFULL

ACCESSION NUMBER: 95:114839 USPATFULL

TITLE: Multimers of the soluble forms of TNF receptors, their preparation and pharmaceutical compositions containing them

INVENTOR(S): Wallach, David, Rehovot, Israel  
Brakebusch, Cord, Braunschweig, Germany, Federal Republic of

PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Rehovot, Israel (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5478925 19951226  
APPLICATION INFO.: US 1992-925687 19920807 (7)

NUMBER DATE

PRIORITY INFORMATION: IL 1991-99120 19910807  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Walsh, Stephen G.  
ASSISTANT EXAMINER: Carlson, K. Cochrane  
LEGAL REPRESENTATIVE: Browdy and Neimark  
NUMBER OF CLAIMS: 7  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 5 Drawing Page(s)  
LINE COUNT: 769

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Multimers of the soluble forms of the tumor necrosis factor receptors (TNF-Rs) are provided. These multimers are produced either by chemical or by recombinant methods. The multimers of the soluble forms of TNF-Rs are useful for protecting mammals (including humans) from the deleterious effects of TNF.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 5 OF 6 CANCERLIT DUPLICATE 2

ACCESSION NUMBER: 94044794 CANCERLIT

DOCUMENT NUMBER: 94044794 PubMed ID: 7693816

TITLE: Expression of a TNF inhibitor in transgenic mice.

AUTHOR: Peppel K; Poltorak A; Melhado I; Jirik F; Beutler B

CORPORATE SOURCE: Howard Hughes Medical Institute, Dallas, TX 75235.

CONTRACT NUMBER: 5-P01-DK42582 (NIDDK)

SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Nov 15) 151 (10) 5699-703.

Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: MEDLINE; Abridged Index Medicus Journals; Priority Journals

OTHER SOURCE: MEDLINE 94044794

ENTRY MONTH: 199312

ENTRY DATE: Entered STN: 19941107

Last Updated on STN: 19960517

AB We previously reported that a chimeric protein consisting of the human p55 TNF receptor covalently linked to a murine IgG1 Fc heavy chain acts as an

efficient TNF inhibitor, as a result of its high binding affinity for native TNF trimers of both murine and human origin. A transgenic mouse line constitutively expressing the inhibitor from a cytomegalovirus promoter was established. All organs examined expressed the transgene. TNF inhibitory activity was easily detected in plasma of transgenic animals but not in plasma of nontransgenic littermates. This founder line was not found to have any obvious phenotype. Specifically, transgenic mice born to wild-type or transgenic females were indistinguishable from nontransgenic littermates with respect to their size at birth, at three months and at six months of age, with respect to the size and morphology of their lymphoid organs and with respect to their hematocrit, white blood cell count, and differential. Although TNF is known to be constitutively expressed by cells of the thymus and trophoblast, the lack of a clear phenotype in association with the constitutive expression of a TNF inhibitor suggests that TNF may be dispensable in early development.

L2 ANSWER 6 OF 6 CANCERLIT DUPLICATE 3  
 ACCESSION NUMBER: 87222282 CANCERLIT  
 DOCUMENT NUMBER: 87222282 PubMed ID: 3034874  
 TITLE: The active form of tumor necrosis factor is a trimer.  
 AUTHOR: Smith R A; Baglioni C  
 CONTRACT NUMBER: CA-29895 (NCI)  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1987 May 25) 262 (15) 6951-4.  
 Journal code: 2985121R. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: MEDLINE; Priority Journals  
 OTHER SOURCE: MEDLINE 87222282  
 ENTRY MONTH: 198706  
 ENTRY DATE: Entered STN: 19941107  
 Last Updated on STN: 19970509

AB Natural human and recombinant human and murine tumor necrosis factors (TNF) were fractionated by gel filtration chromatography on Sephadex G-75. The active form of TNF was identified by its inhibitory activity in receptor binding assays with HeLa cells and was eluted as a protein of Mr approximately 55,000. Radioiodinated human and murine TNF were fractionated by gel filtration into a major peak of Mr approximately 55,000, corresponding to a trimer, and a minor peak of Mr approximately 17,000, corresponding to a monomer. Binding assays showed that the trimer was at least 8-fold more active than the monomer. The human TNF partially dissociated into monomers upon addition of the nonionic detergent Triton X-100. Isolated monomers showed low binding affinity ( $K_D = 70$  nM) and reduced cytotoxicity, whereas trimers showed high binding affinity ( $K_D = 90$  pM) and cytotoxicity. When  $^{125}$ I-TNF was bound to cells, no release of monomer was detectable, suggesting that the trimer could directly bind to cellular receptors without dissociating into subunits. Further evidence for such binding was obtained by cross-linking  $^{125}$ I-TNF trimers with bis[2-(succinimidooxycarbonyloxy)ethyl]sulfone. These trimers were bound to HeLa cells, could be dissociated from cellular receptors, and elicited a cytotoxic response. These results show that trimers, whether native or cross-linked, bind to receptors and are the biologically active form of TNF.

=> s mixed (w) tn timer (w) trimers  
 L3 0 MIXED (W) TNF (W) TRIMERS

=> s mixed (s) tn timer (s) receptor  
 L4 2 MIXED (S) TNF (S) TRIMERS (S) RECEPTOR

=> dl4 1- ibib,abs  
 DL4 IS NOT A RECOGNIZED COMMAND  
 The previous command name entered was not recognized by the system.  
 For a list of commands available to you in the current file, enter  
 "HELP COMMANDS" at an arrow prompt (=>).

=> dl4 1- ibib,abs

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 2 USPATFULL

ACCESSION NUMBER: 2002:206175 USPATFULL

TITLE: Design and discovery of protein based TNF-alpha  
variants for the treatment of TNF-alpha related  
disorders

INVENTOR(S): Dahiyat, Bassil I., Los Angeles, CA, UNITED STATES  
Filikov, Anton, San Diego, CA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2002110868 A1 20020815  
APPLICATION INFO.: US 2001-981289 A1 20011015 (9)  
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-945150, filed  
on 31 Aug 2001, PENDING Continuation-in-part of Ser.  
No. US 2001-798789, filed on 2 Mar 2001, PENDING

NUMBER DATE

PRIORITY INFORMATION: US 2000-186427P 20000302 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: FLEHR HOHBACH TEST, ALBRITTON & HERBERT LLP, Four  
Embarcadero Center, Suite 3400, San Francisco, CA,  
94111

NUMBER OF CLAIMS: 12

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 14 Drawing Page(s)

LINE COUNT: 2937

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel proteins with TNF-.alpha. antagonist  
activity and nucleic acids encoding these proteins. The invention  
further relates to the use of the novel proteins in the treatment of  
TNF-.alpha. related disorders, such as rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 2 OF 2 USPATFULL

ACCESSION NUMBER: 2002:16900 USPATFULL

TITLE: Design and discovery of protein based TNF-alpha  
variants for the treatment of TNF-alpha related  
disorders

INVENTOR(S): Dahiyat, Bassil I., Los Angeles, CA, UNITED STATES  
Filikov, Anton, Monrovia, CA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2002009780 A1 20020124  
APPLICATION INFO.: US 2001-798789 A1 20010302 (9)

NUMBER DATE

PRIORITY INFORMATION: US 2000-186427P 20000302 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP, Four  
Embarcadero Center, Suite 3400, San Francisco, CA,  
94111

NUMBER OF CLAIMS: 13

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 21 Drawing Page(s)

LINE COUNT: 3189

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel proteins with TNF-.alpha. antagonist  
activity and nucleic acids encoding these proteins. The invention  
further relates to the use of the novel proteins in the treatment of  
TNF-.alpha. related disorders, such as rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s mixed (s) tnf (s) trimers  
L5 6 MIXED (S) TNF (S) TRIMERS

=> d l5 1- ibib,abs  
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 6 CANCERLIT  
ACCESSION NUMBER: 2000245895 CANCERLIT  
DOCUMENT NUMBER: 20245895 PubMed ID: 10781424  
TITLE: Human SP-A protein variants derived from one or both genes  
stimulate TNF-alpha production in the THP-1 cell line.  
AUTHOR: Wang G; Phelps D S; Umstead T M; Floros J  
CORPORATE SOURCE: Department of Cellular and Molecular Physiology, The  
Pennsylvania State University College of Medicine, Hershey,  
Pennsylvania 17033, USA.  
CONTRACT NUMBER: HL54683 (NHLBI)  
R01ES09882-01 (NIEHS)  
R37HL34788 (NHLBI)  
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY. LUNG CELLULAR AND MOLECULAR  
PHYSIOLOGY, (2000 May) 278 (5) L946-54.  
Journal code: 100901229. ISSN: 1040-0605.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: MEDLINE; Priority Journals  
OTHER SOURCE: MEDLINE 2000245895  
ENTRY MONTH: 200006  
ENTRY DATE: Entered STN: 20000719  
Last Updated on STN: 20000719

AB In humans, two functional genes of surfactant protein (SP) A, SP-A1 and SP-A2, and several alleles of each functional gene have been characterized. SP-A is a multimeric molecule consisting of six trimers. Each trimer contains two SP-A1 molecules and one SP-A2 molecule. Until now, it has been unclear whether a single SP-A gene product is functional or whether there are functional differences either among alleles or between single-gene SP-A products and SP-A products derived from both genes. We tested the ability of in vitro expressed SP-A variants to stimulate tumor necrosis factor (TNF)-alpha production by THP-1 cells. We observed that 1) single-gene products and products derived from both genes stimulate TNF-alpha production, 2) there are differences among SP-A1 and SP-A2 alleles in their ability to stimulate TNF-alpha production, and 3) the increases in TNF-alpha production are lower after treatment with the SP-A1 alleles than after treatment with the SP-A2 alleles. Furthermore, coexpressed SP-As from SP-A1 and SP-A2 genes have a higher activity compared with SP-As from individual alleles or mixed SP-As from SP-A1 and SP-A2 genes. These data suggest that the SP-A-induced increases in TNF-alpha levels differ among SP-A variants and appear to be affected by SP-A genotype and whether SP-A is derived from one or both genes.

L5 ANSWER 2 OF 6 MEDLINE  
ACCESSION NUMBER: 2000245895 MEDLINE  
DOCUMENT NUMBER: 20245895 PubMed ID: 10781424  
TITLE: Human SP-A protein variants derived from one or both genes  
stimulate TNF-alpha production in the THP-1 cell line.  
AUTHOR: Wang G; Phelps D S; Umstead T M; Floros J  
CORPORATE SOURCE: Department of Cellular and Molecular Physiology, The  
Pennsylvania State University College of Medicine, Hershey,  
Pennsylvania 17033, USA.  
CONTRACT NUMBER: HL54683 (NHLBI)  
R01ES09882-01 (NIEHS)  
R37HL34788 (NHLBI)  
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY. LUNG CELLULAR AND MOLECULAR  
PHYSIOLOGY, (2000 May) 278 (5) L946-54.  
Journal code: 100901229. ISSN: 1040-0605.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200006  
ENTRY DATE: Entered STN: 20000613  
Last Updated on STN: 20000613  
Entered Medline: 20000601

AB In humans, two functional genes of surfactant protein (SP) A, SP-A1 and SP-A2, and several alleles of each functional gene have been characterized. SP-A is a multimeric molecule consisting of six trimers. Each trimer contains two SP-A1 molecules and one SP-A2 molecule. Until now, it has been unclear whether a single SP-A gene product is functional or whether there are functional differences either among alleles or between single-gene SP-A products and SP-A products derived from both genes. We tested the ability of in vitro expressed SP-A variants to stimulate tumor necrosis factor (TNF)-alpha production by THP-1 cells. We observed that 1) single-gene products and products derived from both genes stimulate TNF-alpha production, 2) there are differences among SP-A1 and SP-A2 alleles in their ability to stimulate TNF-alpha production, and 3) the increases in TNF-alpha production are lower after treatment with the SP-A1 alleles than after treatment with the SP-A2 alleles. Furthermore, coexpressed SP-As from SP-A1 and SP-A2 genes have a higher activity compared with SP-As from individual alleles or mixed SP-As from SP-A1 and SP-A2 genes. These data suggest that the SP-A-induced increases in TNF-alpha levels differ among SP-A variants and appear to be affected by SP-A genotype and whether SP-A is derived from one or both genes.

L5 ANSWER 3 OF 6 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000202795 EMBASE

TITLE: Human SP-A protein variants derived from one or both genes stimulate TNF-.alpha. production in the THP-1 cell line.

AUTHOR: Wang G.; Phelps D.S.; Umstead T.M.; Floros J.

CORPORATE SOURCE: J. Floros, Dept. of Cell. and Molec. Physiology, Pennsylvania State Univ., College of Medicine, 500 University Dr., Hershey, PA 17033, United States.  
jxf19@psu.edu

SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2000) 278/5 22-5 (L946-L954).  
Refs: 43

ISSN: 1040-0605 CODEN: APLPE7

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

015 Chest Diseases, Thoracic Surgery and Tuberculosis

026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB In humans, two functional genes of surfactant protein (SP) A, SP-A1 and SP-A2, and several alleles of each functional gene have been characterized. SP-A is a multimeric molecule consisting of six trimers. Each trimer contains two SP-A1 molecules and one SP-A2 molecule. Until now, it has been unclear whether a single SP-A gene product is functional or whether there are functional differences either among alleles or between single-gene SP-A products and SP-A products derived from both genes. We tested the ability of in vitro expressed SP-A variants to stimulate tumor necrosis factor (TNF)-.alpha. production by THP-1 cells. We observed that 1) single-gene products and products derived from both genes stimulate TNF-.alpha. production, 2) there are differences among SP-A1 and SP-A2 alleles in their ability to stimulate TNF-.alpha. production, and 3) the increases in TNF-.alpha. production are lower after treatment with the SP-A1 alleles than after treatment with the SP-A2 alleles. Furthermore, coexpressed SP-As from SP-A1 and SP-A2 genes have a higher activity compared with SP-As from individual alleles or mixed SP-As from SP- A1 and SP-A2 genes. These data suggest that the SP-A-induced increases in TNF-X.alpha. levels differ among SP-A variants and appear to be affected by SP-A genotype and whether SP-A is derived from one or both genes.

L5 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:302825 BIOSIS

DOCUMENT NUMBER: PREV200000302825

TITLE: Human SP-A protein variants derived from one or both genes  
stimulate TNF-alpha production in the THP-1 cell line.

AUTHOR(S): Wang, Guirong; Phelps, David S.; Umstead, Todd M.; Floros,  
Joanna (1)

CORPORATE SOURCE: (1) Dept. of Cellular and Molecular Physiology (H166),  
Pennsylvania State Univ. College of Medicine, 500  
University Dr., Hershey, PA, 17033 USA

SOURCE: American Journal of Physiology, (May, 2000) Vol. 278, No. 5  
part 1, pp. L946-L954. print.  
ISSN: 0002-9513.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB In humans, two functional genes of surfactant protein (SP) A, SP-A1 and  
SP-A2, and several alleles of each functional gene have been  
characterized. SP-A is a multimeric molecule consisting of six  
trimers. Each trimer contains two SP-A1 molecules and one SP-A2  
molecule. Until now, it has been unclear whether a single SP-A gene  
product is functional or whether there are functional differences either  
among alleles or between single-gene SP-A products and SP-A products  
derived from both genes. We tested the ability of in vitro expressed SP-A  
variants to stimulate tumor necrosis factor (TNF)-alpha  
production by THP-1 cells. We observed that 1) single-gene products and  
products derived from both genes stimulate TNF-alpha production,  
2) there are differences among SP-A1 and SP-A2 alleles in their ability to  
stimulate TNF-alpha production, and 3) the increases in  
TNF-alpha production are lower after treatment with the SP-A1  
alleles than after treatment with the SP-A2 alleles. Furthermore,  
coexpressed SP-As from SP-A1 and SP-A2 genes have a higher activity  
compared with SP-As from individual alleles or mixed SP-As from  
SP-A1 and SP-A2 genes. These data suggest that the SP-A-induced increases  
in TNF-alpha levels differ among SP-A variants and appear to be  
affected by SP-A genotype and whether SP-A is derived from one or both  
genes.

L5 ANSWER 5 OF 6 USPATFULL

ACCESSION NUMBER: 2002:206175 USPATFULL

TITLE: Design and discovery of protein based TNF-alpha  
variants for the treatment of TNF-alpha related  
disorders

INVENTOR(S): Dahiyat, Bassil I., Los Angeles, CA, UNITED STATES  
Filikov, Anton, San Diego, CA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2002110868 A1 20020815

APPLICATION INFO.: US 2001-981289 A1 20011015 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-945150, filed  
on 31 Aug 2001, PENDING Continuation-in-part of Ser.  
No. US 2001-798789, filed on 2 Mar 2001, PENDING

NUMBER DATE

PRIORITY INFORMATION: US 2000-186427P 20000302 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: FLEHR HOHBACH TEST, ALBRITTON & HERBERT LLP, Four  
Embarcadero Center, Suite 3400, San Francisco, CA,  
94111

NUMBER OF CLAIMS: 12

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 14 Drawing Page(s)

LINE COUNT: 2937

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel proteins with TNF-.alpha. antagonist  
activity and nucleic acids encoding these proteins. The invention  
further relates to the use of the novel proteins in the treatment of



TNF-.alpha. related disorders, such as rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 6 USPATFULL

ACCESSION NUMBER: 2002:16900 USPATFULL

TITLE: Design and discovery of protein based TNF-alpha  
variants for the treatment of TNF-alpha related  
disorders

INVENTOR(S): Dahiyat, Bassil I., Los Angeles, CA, UNITED STATES  
Filikov, Anton, Monrovia, CA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2002009780 A1 20020124

APPLICATION INFO.: US 2001-798789 A1 20010302 (9)

NUMBER DATE

PRIORITY INFORMATION: US 2000-186427P 20000302 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP, Four  
Embarcadero Center, Suite 3400, San Francisco, CA,  
94111

NUMBER OF CLAIMS: 13

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 21 Drawing Page(s)

LINE COUNT: 3189

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel proteins with TNF-.alpha. antagonist  
activity and nucleic acids encoding these proteins. The invention  
further relates to the use of the novel proteins in the treatment of  
TNF-.alpha. related disorders, such as rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.